

Document made available under the Patent Cooperation Treaty (PCT)

International application number: PCT/US05/004291

International filing date: 11 February 2005 (11.02.2005)

Document type: Certified copy of priority document

Document details: Country/Office: US
Number: 60/544,171
Filing date: 11 February 2004 (11.02.2004)

Date of receipt at the International Bureau: 11 March 2005 (11.03.2005)

Remark: Priority document submitted or transmitted to the International Bureau in compliance with Rule 17.1(a) or (b)



World Intellectual Property Organization (WIPO) - Geneva, Switzerland
Organisation Mondiale de la Propriété Intellectuelle (OMPI) - Genève, Suisse

1290494

THE UNITED STATES OF AMERICA

TO ALL TO WHOM THESE PRESENTS SHALL COME:

UNITED STATES DEPARTMENT OF COMMERCE

United States Patent and Trademark Office

March 01, 2005

THIS IS TO CERTIFY THAT ANNEXED HERETO IS A TRUE COPY FROM THE RECORDS OF THE UNITED STATES PATENT AND TRADEMARK OFFICE OF THOSE PAPERS OF THE BELOW IDENTIFIED PATENT APPLICATION THAT MET THE REQUIREMENTS TO BE GRANTED A FILING DATE.

APPLICATION NUMBER: 60/544,171

FILING DATE: February 11, 2004

RELATED PCT APPLICATION NUMBER: PCT/US05/04291



Certified by

Under Secretary of Commerce
for Intellectual Property
and Director of the United States
Patent and Trademark Office

Please type a plus sign (+) inside this box ☐

PTO/SB/16 (5-03)
Approved for use through 4/30/2003. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

PROVISIONAL APPLICATION FOR PATENT COVER SHEET

This is a request for filing a PROVISIONAL APPLICATION FOR PATENT under 37 CFR 1.53(c).

INVENTOR(S)					
Given Name (first and middle [if any])		Family Name or Surname		Residence (City and either State or Foreign Country)	
Sanjaya Subramaniam C. David Noah		Khanal Krishnan Kenigsberg		Detroit, Michigan Detroit, Michigan Detroit, Michigan	
<input type="checkbox"/> Additional inventors are being named on the _____ separately numbered sheets attached hereto					
TITLE OF THE INVENTION (280 characters max)					
METHOD AND DEVICE FOR DETECTING PROLONGED CARDIAC REPOLARIZATION TO DIAGNOSE TRANSMURAL MYOCARDIAL ISCHEMIA					
Direct all correspondence to: CORRESPONDENCE ADDRESS					
<input type="checkbox"/> Customer Number		<input type="text"/>		<div>Place Customer Number Bar Code Label here</div>	
OR Type Customer Number here					
<input checked="" type="checkbox"/> Firm or Individual Name		KOHN & ASSOCIATES, PLLC			
Address					
Address		30500 Northwestern Highway, Suite 410			
City		Farmington Hills	State	Michigan	ZIP 48334
Country		US	Telephone	(248) 539-5050	Fax (248) 539-5055
ENCLOSED APPLICATION PARTS (check all that apply)					
<input checked="" type="checkbox"/> Specification Number of Pages		11		<input type="checkbox"/> CD(s), Number <input type="text"/>	
<input type="checkbox"/> Drawing(s) Number of Sheets		<input type="text"/>		<input checked="" type="checkbox"/> Other (specify)	
<input type="checkbox"/> Application Data Sheet. See 37 CFR 1.76		<div>Acknowledgement Postcard</div>			
METHOD OF PAYMENT OF FILING FEES FOR THIS PROVISIONAL APPLICATION FOR PATENT (check one)					
<input checked="" type="checkbox"/> Applicant claims small entity status. See 37 CFR 1.27.				FILING FEE AMOUNT (\$)	
<input checked="" type="checkbox"/> A check or money order is enclosed to cover the filing fees					
<input checked="" type="checkbox"/> The Director is hereby authorized to charge filing fees or credit any overpayment to Deposit Account Number		11-1449		\$80.00	
<input type="checkbox"/> Payment by credit card. Form PTO-2038 is attached.					
The invention was made by an agency of the United States Government or under a contract with an agency of the United States Government.					
<input checked="" type="checkbox"/> No.					
<input type="checkbox"/> Yes, the name of the U.S. Government agency and the Government contract number are: _____					

Respectfully submitted,

SIGNATURE

Date

2-11-04

TYPED or PRINTED NAME

Amy E. Rinaldo

REGISTRATION NO.

45,791

(if appropriate)

Docket Number:

1059.00098

TELEPHONE

(248) 539-5050

USE ONLY FOR FILING A PROVISIONAL APPLICATION FOR PATENT

This collection of information is required by 37 CFR 1.51. The information is used by the public to file (and by the PTO to process) a provisional application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 8 hours to complete, including gathering, preparing, and submitting the complete provisional application to the PTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Mail Stop Provisional Application, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

P19SMALL/REV05

Attorney Docket No: 105900098

Express Mail Number: EV 407003325 US

PROVISIONAL PATENT APPLICATION

METHOD AND DEVICE FOR DETECTING PROLONGED CARDIAC REPOLARIZATION TO DIAGNOSE TRANSMURAL MYOCARDIAL ISCHEMIA

BACKGROUND OF THE INVENTION

1. Technical Field

The present invention relates to a device and method for detecting prolongation of myocardial repolarization as a novel marker of transmural ischemia. More specifically, the present invention provides a method and device to detect prolonged repolarization using electrocardiographic and electrophysiological tools and measurements to make the diagnosis of transmural ischemia.

2. Description of the Related Art

Many cardiac conditions can be detected by measuring and recording

electrical signals from the heart. When displayed, the electrical signals form various patterns, which can be visually recognized. Generally, the electrical signal recorded from the ventricle or the atrium of the heart has different components: a sharper high frequency component that represents "depolarization" of the heart muscle and slower frequencies that represent the "repolarization" component. Electrocardiograms are routinely used for diagnosis and therapy of various cardiac conditions, based on certain patterns of abnormalities seen in the depolarization or the repolarization components of the ECG. However, the electrocardiograms measured and used in the usually described format have significant limitations in detecting and identifying cardiac ischemia. Transmural ischemia is currently identified electrocardiographically by analyzing the QRS, ST and T-waves morphology. However, the changes in these electrocardiographic signals are neither sensitive nor specific in detecting transmural ischemia.¹

Additionally, the waveforms are often not able to detect the occurrence of transmural ischemia, because depending upon the timing of the ECG, classical changes, such as ST segment elevation or Q waves, may be absent. As a result, many individuals may be experiencing transmural ischemia, but are never diagnosed. It would therefore be beneficial to develop a method and device for detecting the occurrence of transmural ischemia by measuring the duration of myocardial repolarization.

DESCRIPTION OF THE INVENTION

Generally, the present invention provides a method and device for the detection of prolonged myocardial repolarization that, as we have shown, can be used to diagnose even brief episodes of transmural ischemia (<2minutes). More specifically, the present invention provides a device to measure the duration of myocardial repolarization during transmural ischemia or infarction.

The device of the present invention can be any device, be it automated or manual, that is capable of accurately measuring the QT interval and other indices of measuring the duration of myocardial repolarization. Classical cardiology and physiology teachings state that the metabolic changes that occur in ischemic hearts promote the abbreviation of the myocardial repolarization and the QT interval.^{2, 3} On the contrary, the current invention detects a paradoxical prolongation of the QT interval and duration of myocardial repolarization as a marker of transmural ischemia. It has been determined by Applicants that prolongation of the QTc and duration of myocardial repolarization occurs prior to other changes during acute transmural ischemia. The prolongation of the QT interval is one of the first detectable symptoms of transmural ischemia. It is also the most consistent finding (occurring in 100% of patients).

The corrected QT interval on the surface electrocardiogram is the

earliest and most consistent (100%) finding during transmural ischemia induced by balloon occlusion during percutaneous coronary angioplasty. This should be contrasted with the fact that in the study, substantially fewer numbers of patients developed chest pain (33%) or ST segment elevation (50%), the classical electrocardiographic feature of transmural myocardial ischemia.

The QT interval is the measure of repolarization of the ventricular electrical signal on the surface electrocardiogram. In addition, other methods to assess repolarization include intracardiac electrograms, assessing activation recovery intervals and monophasic action potentials.

During a myocardial infarction intermittent occlusion can occur, resulting in cyclical flow, resulting in the absence of classical ECG changes. Any technology incorporated into any external (wearable monitor), internal (implantable) or intracardiac devices (using QT/QTc intervals, activation recovery intervals, monophasic action potential durations) can be used to accurately measure repolarization times and thus enhance the sensitivity in detecting transmural myocardial ischemia.^{4,5}

Additionally, prolongation of the repolarization time after balloon inflation during percutaneous coronary intervention may be used to determine the status of the microvasculature and myocardial perfusion i.e. if there is a

long delay in return of the QT to baseline, it may indicate occurrence of embolization of atherosclerotic or thrombotic material downstream from the balloon inflation and certain therapeutic measures can therefore be instituted.

More specifically, the device of the present invention functions by reviewing the QT interval of the ECG and various indices of myocardial repolarization. Then the device quantitates the QT interval or duration of myocardial repolarization and compares the results with a standard to determine if there is deviation from the standard and tracks changes over time. Specifically, if the device detects a prolongation of the QT interval it is indicative of transmural ischemia.

The present invention can be included in a portable device that is worn by an individual. The device can be worn by an individual in order to detect ischemia. Alternatively, the device can be located at a hospital or doctor's office. It can also be incorporated into a device implanted in the body. The device can be used to detect ischemia in patient's presenting with or without symptoms. It can also be used in monitoring high risk patients for early transmural ischemia.

Throughout this application, author and year, and patents, by number, reference various publications, including United States patents. Full citations for the publications are listed below. The disclosures of these publications

and patents in their entireties are hereby incorporated by reference into this application in order to more fully describe the state of the art to which this invention pertains.

The invention has been described in an illustrative manner, and it is to be understood that the terminology that has been used is intended to be in the nature of words of description rather than of limitation.

Obviously, many modifications and variations of the present invention are possible in light of the above teachings. It is, therefore, to be understood that within the scope of the described invention, the invention may be practiced otherwise than as specifically described.

References:

1. ST-Segment Elevation in Conditions Other Than Acute Myocardial Infarction. Wang K., Asinger R.W., Marriott H. J.L. N Engl J Med. 349:2128-2135, Nov 27, 2003.
2. Russel DC, Smith HJ, Oliver MF: Transmembrane potential changes and ventricular fibrillation during repetitive myocardial ischemia in the dog. British Heart Journal 1979; 42:88-96
3. Weidman S: Elektrophysiologie der Herzmuskelfaser. Huber, Bern, 1956.
4. Haws CW, Lux RL. Correlation between in vivo transmembrane action potential durations and activation-recovery intervals from electrograms: effects of interventions that alter repolarization time. *Circulation*. 1990; 81:281–288.
5. Wyatt R. Comparison of estimates of activation and recovery times from bipolar and unipolar electrograms to in vivo transmembrane action potential duration. In: *Proceedings IEE: Engineering Medical Biologists Society Second Annual Conference*. Washington, DC; 1980:22.